CAV3 gene

caveolin 3

Normal Function

The *CAV3* gene provides instructions for making a protein called caveolin-3, which is found in the membrane surrounding muscle cells. This protein is the main component of caveolae, which are small pouches in the muscle cell membrane. Within the caveolae, the caveolin-3 protein acts as a scaffold to organize other molecules that are important for cell signaling and maintenance of the cell structure. These molecules include the proteins that make up sodium channels, which transport positively charged sodium atoms (sodium ions) into cells. Sodium channels play a key role in a cell's ability to generate and transmit electrical signals. In cardiac muscle, sodium channels are involved in maintaining the heart's normal rhythm. Caveolin-3 may also help regulate calcium levels in the muscle cell, which control muscle contraction and relaxation.

Health Conditions Related to Genetic Changes

CAV3-related distal myopathy

At least two *CAV3* gene mutations have been identified in people with distal myopathy, a disorder characterized by weakness and loss of function mainly affecting the muscles farthest from the center of the body (distal muscles), such as those of the hands and feet. Mutations that cause *CAV3*-related distal myopathy result in a shortage of caveolin-3 protein in the muscle cell membrane and a reduction in the number of caveolae. Researchers suggest that a shortage of caveolae impairs the structural integrity of muscle cells, interferes with cell signaling, and causes the self-destruction of cells (apoptosis). The resulting breakdown of muscle tissue leads to the signs and symptoms of *CAV3*-related distal myopathy.

isolated hyperCKemia

At least four *CAV3* gene mutations have been identified in individuals with isolated hyperCKemia. People with this condition have elevated levels of an enzyme called creatine kinase in the blood. Creatine kinase is released into the blood when muscle cells are damaged; however, people with isolated hyperCKemia have no muscle weakness or other symptoms of muscle disease. *CAV3* gene mutations that cause isolated hyperCKemia lead to a caveolin-3 shortage that likely damages muscle cells. Although the damage is not severe enough to cause noticeable symptoms, it may lead to the elevated blood levels of creatine kinase that characterize isolated hyperCKemia.

limb-girdle muscular dystrophy

More than 20 mutations in the *CAV3* gene have been identified in people with limb-girdle muscular dystrophy type 1C. Limb-girdle muscular dystrophy is a group of related disorders characterized by muscle weakness and wasting, particularly in the shoulders, hips, and limbs.

As in *CAV3*-related distal myopathy (described above), *CAV3* gene mutations that cause limb-girdle muscular dystrophy type 1C result in a shortage of caveolin-3 protein that damages muscle tissue, leading to the signs and symptoms of this disorder.

rippling muscle disease

At least 12 *CAV3* gene mutations have been identified in people with rippling muscle disease, a condition in which the muscles are unusually sensitive to movement or pressure (irritable). Affected individuals may have muscle cramps, stiffness, and muscles that appear to ripple when they are stretched.

CAV3 gene mutations that cause rippling muscle disease result in a shortage of caveolin-3 protein in the muscle cell membrane. Researchers suggest that reduced caveolin-3 levels may impair the control of calcium levels in muscle cells, leading to abnormal muscle contractions in response to stimulation.

other disorders

CAV3 gene mutations also can cause hypertrophic cardiomyopathy. Hypertrophic cardiomyopathy is a thickening of the heart (cardiac) muscle that forces the heart to work harder to pump blood. This condition can lead to heart failure.

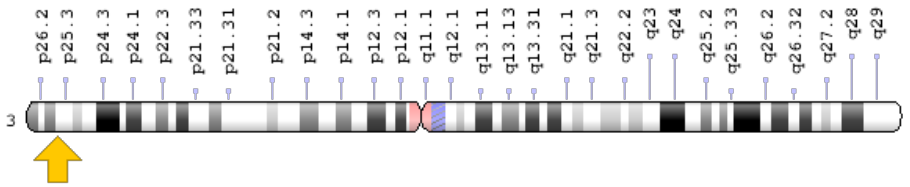
When caused by *CAV3* gene mutations, hypertrophic cardiomyopathy as well as limb-girdle muscular dystrophy, isolated hyperCKemia, rippling muscle disease, and distal myopathy (all described above) are classified as caveolinopathies. Several *CAV3* gene mutations have been found to cause different caveolinopathies in different individuals. It is unclear why a particular *CAV3* gene mutation may cause different patterns of signs and symptoms, even within the same family.

Mutations in the *CAV3* gene have also been identified in people with long QT syndrome, which is a heart condition that causes the cardiac muscle to take longer than usual to recharge between beats. The irregular heartbeats (arrhythmia) can lead to fainting (syncope) or cardiac arrest and sudden death. Researchers suggest that *CAV3* gene mutations may disrupt ion transport through sodium channels located in the caveolae. A disruption in ion transport may alter the way the heart beats, leading to the abnormal heart rhythm characteristic of long QT syndrome.

Chromosomal Location

Cytogenetic Location: 3p25.3, which is the short (p) arm of chromosome 3 at position 25.3

Molecular Location: base pairs 8,733,800 to 8,746,765 on chromosome 3 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CAV3_HUMAN
- caveolin-3
- LGMD1C
- LQT9
- M-caveolin
- MGC126100
- MGC126101
- MGC126129
- VIP-21
- VIP21

Additional Information & Resources

Educational Resources

- University of Washington Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/musdist/lg.html#cav3var

GeneReviews

- Caveolinopathies
  https://www.ncbi.nlm.nih.gov/books/NBK1385

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CAV3%5BTIAB%5D%29+OR+%28caveolin+3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- CAVEOLIN 3
  http://omim.org/entry/601253
- LONG QT SYNDROME 9
  http://omim.org/entry/611818

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_CAV3.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CAV3%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=1529
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/859
- UniProt
  http://www.uniprot.org/uniprot/P56539

Sources for This Summary

- Aboumousa A, Hoogendijk J, Charlton R, Barresi R, Herrmann R, Voit T, Hudson J, Roberts M, Hilton-Jones D, Eagle M, Bushby K, Straub V. Caveolinopathy--new mutations and additional symptoms. Neuromuscul Disord. 2008 Jul;18(7):572-8. doi: 10.1016/j.nmd.2008.05.003. Epub 2008 Jun 25.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18583131
- Alias L, Gallano P, Moreno D, Pujol R, Martínez-Matos JA, Baiget M, Ferrer I, Olivé M. A novel mutation in the caveolin-3 gene causing familial isolated hyperCKaemia. Neuromuscul Disord. 2004 May;14(5):321-4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15099591
- Balijepalli RC, Kamp TJ. Caveolae, ion channels and cardiac arrhythmias. Prog Biophys Mol Biol. 2008 Oct-Nov;98(2-3):149-60. doi: 10.1016/j.pbiomolbio.2009.01.012. Epub 2009 Jan 30. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19351512
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2836876/

- OMIM: CAVEOLIN 3
  http://omim.org/entry/601253
- Catteruccia M, Sanna T, Santorelli FM, Tessa A, Di Giacopo R, Sauchelli D, Verbo A, Lo Monaco M, Servidei S. Rippling muscle disease and cardiomyopathy associated with a mutation in the CAV3 gene. Neuromuscul Disord. 2009 Nov;19(11):779-83. doi: 10.1016/j.nmd.2009.08.015. Epub 2009 Sep 20.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19773168
- Gazzerro E, Bonetto A, Minetti C. Caveolinopathies: translational implications of caveolin-3 in skeletal and cardiac muscle disorders. Handb Clin Neurol. 2011;101:135-42. doi: 10.1016/B978-0-08-045031-5.00010-4. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21496630
- Gazzerro E, Sotgia F, Bruno C, Lisanti MP, Minetti C. Caveolinopathies: from the biology of caveolin-3 to human diseases. Eur J Hum Genet. 2010 Feb;18(2):137-45. doi: 10.1038/ejhg.2009.103. Epub 2009 Jul 8. Review. Erratum in: Eur J Hum Genet. 2009 Dec;17(12):1692.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19584897
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2987183/
- Tateyama M, Aoki M, Nishino I, Hayashi YK, Sekiguchi S, Shiga Y, Takahashi T, Onodera Y, Haginoya K, Kobayashi K, Iinuma K, Nonaka I, Arahata K, Itoyama Y. Mutation in the caveolin-3 gene causes a peculiar form of distal myopathy. Neurology. 2002 Jan 22;58(2):323-5. Erratum in: Neurology 2002 Mar 12;58(5):839. Itoyoma Y [corrected to Itoyama Y].
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11805270
- Traverso M, Bruno C, Broccolini A, Sotgia F, Donati MA, Assereto S, Gazzerro E, Lo Monaco M, Modoni A, D'Amico A, Gasperini S, Ricci E, Zara F, Lisanti M, Minetti C. Truncation of Caveolin-3 causes autosomal-recessive Rippling Muscle Disease. J Neurol Neurosurg Psychiatry. 2008 Jun;79(6):735-7. doi: 10.1136/jnnp.2007.133207.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18487559
- Ullrich ND, Fischer D, Kornblum C, Walter MC, Niggli E, Zorzato F, Treves S. Alterations of excitation-contraction coupling and excitation coupled Ca(2+) entry in human myotubes carrying CAV3 mutations linked to rippling muscle. Hum Mutat. 2011 Mar;32(3):309-17. doi: 10.1002/humu.21431. Epub 2011 Feb 3.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21294223
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3132216/
- Vatta M, Ackerman MJ, Ye B, Makielski JC, Ughanze EE, Taylor EW, Tester DJ, Balijepalli RC, Foell JD, Li Z, Kamp TJ, Towbin JA. Mutant caveolin-3 induces persistent late sodium current and is associated with long-QT syndrome. Circulation. 2006 Nov 14;114(20):2104-12. Epub 2006 Oct 23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17060380

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